

WHAT IS CLAIMED IS:

1 1. A method of correlating gene and protein expression in a biological
2 sample, the method comprising the steps of:

3 a) obtaining the biological sample ;

4 b) generating a gene expression profile of the sample, thereby identifying
5 an mRNA expressed in the sample;

6 c) identifying a physio-chemical property of a polypeptide encoded by the
7 mRNA;

8 d) fractionating polypeptides in the sample on the basis of the physio-
9 chemical property and;

10 (e) identifying the polypeptide encoded by the mRNA from among the
11 fractionated proteins, wherein the identified polypeptide comprises the physio-chemical
12 property;

13 thereby correlating gene and protein expression in the sample.

1 2. The method of claim 1, wherein the biological sample comprises a
2 cell lysate from a healthy cell.

1 3. The method of claim 1, wherein the biological sample comprises a
2 cell lysate from a pathological cell.

1 4. The method of claim 1, wherein the biological sample comprises a
2 cell lysate from a cell contacted by a toxic compound.

1 5. The method of claim 1, wherein the biological sample comprises a
2 cell lysate from a cell of a subject who respond to a drug treatment or a subject who does
3 not respond to a drug treatment.

1 6. The method of claim 1, wherein the biological sample comprises a
2 cell lysate from a cell exposed to heat, cold, or radiation.

1 7. The method of claim 1, wherein the biological sample comprises a
2 human cell.

1 8. The method of claim 1, wherein the step of generating the gene
2 expression profile comprises identifying expressed mRNA with an EST array.

1 9. The method of claim 1, wherein the step of generating the gene
2 expression profile comprises identifying expressed mRNA with an oligonucleotide array.

1 10. The method of claim 1, wherein the step of generating the gene
2 expression profile comprises identifying expressed mRNA with an mRNA array.

1 11. The method of claim 1, wherein the mRNA is differentially
2 expressed in two biological samples.

1 12. The method of claim 11, wherein the two biological samples are
2 derived from a normal cell and a pathologic cell.

1 13. The method of claim 12, wherein the pathologic cell is a cancer
2 cell.

1 14. The method of claim 11, wherein the two biological samples are
2 derived from a healthy cell and a cell exposed to a toxic compound.

1 15. The method of claim 1, wherein the step of identifying the physio-
2 chemical property of the polypeptide encoded by the mRNA further comprises
3 identifying a plurality of physio-chemical properties.

1 16. The method of claim 1, wherein the step of identifying a physio-
2 chemical property comprises predicting the masses of proteolytic fragments generated by
3 the polypeptide encoded by the mRNA upon degradation of the polypeptide by a selected
4 proteolytic agent, and the step of identifying the polypeptide encoded by the mRNA
5 comprises subjecting polypeptides in the sample to degradation by the agent and
6 identifying actual proteolytic fragments in the sample having masses that correspond to
7 the masses of the predicted fragments.

1 17. The method of claim 1, wherein the physio-chemical property is
2 selected from the group consisting of: amino acid sequence, molecular weight, iso-
3 electric point, hydrophobicity, hydrophilicity, glycosylation, phosphorylation, epitope
4 sequence, ligand binding sequence, charge at a specified pH, and metal chelate binding.

1 18. The method of claim 1, wherein the step of fractionating the
2 polypeptides in the sample comprises 2D-gel electrophoresis.

19. The method of claim 1, wherein the step of fractionating the polypeptides in the sample comprises mass spectrometry.

20. The method of claim 1, wherein the step of fractionating the polypeptides in the sample comprises surface enhanced laser desorption ionization, wherein the surface enhanced laser desorption ionization comprises fractionating by affinity retention on solid phase-bound adsorbent followed by fractionating retained polypeptides from the solid phase by gas phase ion spectrometry.

21. The method of claim 20, wherein the adsorbent is selected to have affinity for polypeptides possessing at least one physio-chemical property selected from the group consisting of: amino acid sequence, molecular weight, iso-electric point, hydrophobicity, hydrophilicity, glycosylation, phosphorylation, epitope sequence, ligand binding sequence, charge at a specified pH, and metal chelate binding.

22. The method of claim 1, wherein the step of identifying the polypeptide comprises selecting a polypeptide from among the fractionated polypeptides, which selected polypeptide comprises the physio-chemical property, identifying the selected polypeptide and correlating the identity of the selected polypeptide with the polypeptide encoded by the mRNA.

23. A method of correlating gene and protein expression in a biological sample, the method comprising the steps of:

- a) obtaining a biological sample;
 - b) generating a gene expression profile of the sample using a nucleic acid array, thereby identifying an mRNA expressed in the sample;
 - c) identifying a physio-chemical property of a polypeptide encoded by the mRNA;
 - d) fractionating polypeptides in the sample on the basis of the physio-chemical property, using mass spectrometry and;
 - (e) identifying the polypeptide encoded by the mRNA from among the fractionated proteins, wherein the identified polypeptide comprises the physio-chemical property;
- thereby correlating gene and protein expression in the cell.

24. The method of claim 23, wherein the step of generating the gene expression profile comprises identifying expressed mRNA with an EST array.

25. The method of claim 23, wherein the step of generating the gene expression profile comprises identifying expressed mRNA with an oligonucleotide array.

26. The method of claim 23, wherein the step of generating the gene expression profile comprises identifying expressed mRNA with an mRNA array.

27. The method of claim 23, wherein the step of identifying the polypeptide encoded by the mRNA comprises fractionating polypeptides in the sample by surface enhanced laser desorption ionization, wherein the surface enhanced laser desorption ionization comprises fractionating by affinity retention on solid phase-bound adsorbent followed by fractionating retained polypeptides from the solid phase by gas phase ion spectrometry.

28. A method of correlating gene and protein expression in a biological sample, the method comprising the steps of:

a) obtaining a biological sample;
b) generating a gene expression profile of the sample using an oligonucleotide array, thereby identifying an mRNA expressed in the sample;
c) identifying a physio-chemical property of a polypeptide encoded by the mRNA;

d) fractionating polypeptides in the sample on the basis of the physio-chemical property with surface enhanced laser desorption ionization, wherein the surface enhanced laser desorption ionization comprises fractionating by affinity retention on solid phase-bound adsorbent followed by fractionating retained polypeptides from the solid phase by gas phase ion spectrometry; and

e) identifying the polypeptide encoded by the mRNA from among the fractionated proteins, wherein the identified polypeptide comprises the physio-chemical property;

thereby correlating gene and protein expression in the cell.

29. The method of claim 28, wherein the adsorbent is selected to have affinity for polypeptides possessing at least one physio-chemical property selected from

the group consisting of: amino acid sequence, molecular weight, iso-electric point, hydrophobicity, hydrophilicity, glycosylation, phosphorylation, epitope sequence, ligand binding sequence, charge at a specified pH, and metal chelate binding.

30. The method of claim 28, wherein the step of identifying the physio-chemical property comprises predicting the masses of proteolytic fragments generated by the polypeptide encoded by the mRNA upon degradation of the polypeptide by a selected proteolytic agent, and the step of identifying the polypeptide encoded by the mRNA comprises subjecting polypeptides in the sample to degradation by the agent and identifying actual proteolytic fragments in the sample having masses that correspond to the masses of the predicted fragments.